The Role of Academia in Early Drug Development: From Basic Research to Industrial Translation

Contribuciones de la academia al desarrollo temprano de fármacos: de la ciencia básica a la aplicación industrial

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ABSTRACT

This article examines the role of academia in early-stage drug development, from basic research to industrial translation. Through a targeted bibliographic review, it describes strategies such as phenotypic, virtual, and fragment-based screening, rational design, computational modeling, in silico pharmacokinetics, and preclinical testing. The analysis identifies methodological gaps, lack of standardization, and insufficient collaboration with industry as key barriers to translational progress. It concludes that early engagement between academia and industry, along with improved coordination of scientific efforts, is essential to accelerate therapeutic innovation and translate research findings into tangible public health benefits.

Keywords: drug development, drug design, drug discovery.

RESUMEN

Se analiza el papel de la academia en el desarrollo temprano de fármacos. El análisis abarca desde la investigación básica hasta su aplicación industrial. A partir de una búsqueda bibliográfica especializada, se describen estrategias como el cribado fenotípico, virtual y por fragmentos, el diseño racional, el modelado computacional, la predicción farmacocinética *in silico* y los ensayos preclínicos. Se identifican limitaciones metodológicas, falta de estandarización e insuficiente interacción con la industria, factores que dificultan el avance traslacional. Se concluye que una colaboración temprana entre academia e industria y una mejor organización del trabajo científico son esenciales para acelerar la innovación terapéutica y transformar los hallazgos en beneficios concretos para la salud pública.

Palabras clave: desarrollo de medicamentos, descubrimiento de fármacos, diseño de fármacos.

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Introduction

Drug development is a complex and multifaceted process that spans from the identification of molecules with therapeutic potential to the commercialization of the medication. This process can be divided into two main stages: drug discovery and drug development. Drug discovery involves identifying new molecules that can interact with specific biological targets to produce a therapeutic effect. This stage includes basic research, target selection, compound screening, and hit optimization. On the other hand, drug development focuses on transforming these promising compounds into safe and effective pharmaceutical products. This stage encompasses preclinical studies, clinical trials, drug formulation, and the regulatory approval process. It is crucial to understand that while these stages are interrelated, each has its specific challenges and requirements. Collaboration between academia and industry is crucial for overcoming these challenges and advancing the development of new treatments (figure 1).

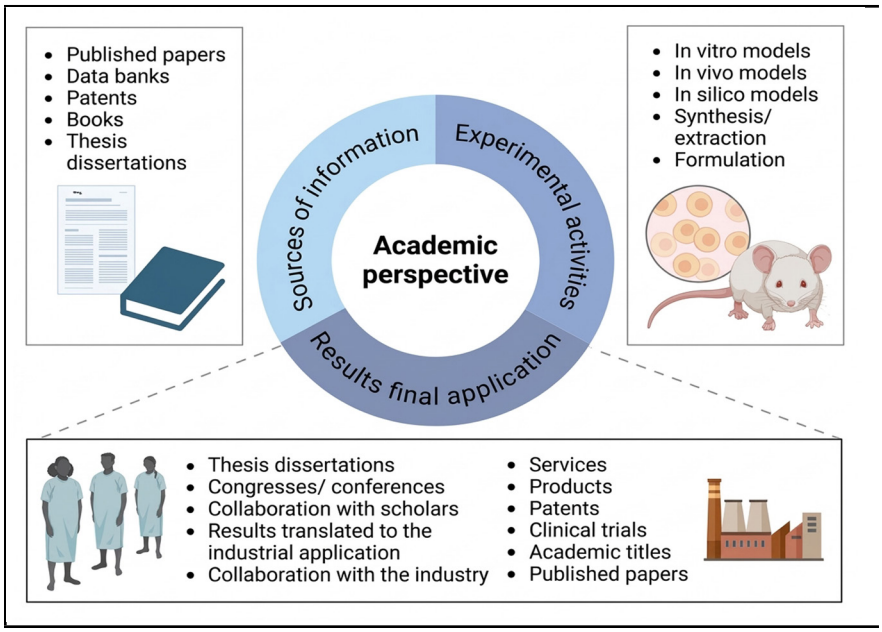

FIGURE 1
Academic perspective of drug development

Source: developed by the author and created using BioRender.
Note: Research in the academic field encompasses all sources of information accessible to the researcher, including experimental activities in the laboratory or based on computational methodologies. The results obtained from the dedicated research time can be applied in a wide variety of forms, some of which are listed in the figure. ▲

The pathway from discovering a molecule with potential therapeutic effects to making it available for patients is far from straightforward. Numerous variables must be considered at each stage of the process. One reason why developing a new drug is a multimillion-dollar endeavor is that it typically takes around 10 years to progress from the lab to pharmacies. Even after all that effort, some drugs are withdrawn from the market due to flaws in critical steps of their

development. From an academic perspective, the focus is on improving the early stages of drug development. This involves utilizing all available laboratory tools and providing scientists with the time and resources needed to explore novel approaches to rational drug design and hit optimization.

1. A first approach to drug discovery

1. 1. Research and data bank screening

The first step in drug discovery is to set a goal by focusing on a specific disease target, structure, or compound. To reach that starting point, it is necessary to explore the state-of-the-art, novel therapies and identify areas of opportunity based on the limitations of commonly used and commercialized drugs (table 1). Several databases now provide data on drug-target interactions, each with different scopes, including: Caroline dos Santos Picanço et al. (2018), such as canSAR (Mitsopoulos et al., 2021), companion diagnostic test, DRD2/DRD3-GTEx (GTEx Portal, 2023), DrugCentral (DrugCentral, 2023), illuminating the druggable genome (IDG, 2023), IUPHAR/BPS Guide to PHARMACOLOGY (2023), NCATS pharmaceutical collection (NCATS, 2023), R project for statistical computing, WHO collaborating centre for drug statistics methodology-ATC/DDD index (NIP. Norwegian Institute of Public Health, 2023), WHO INN drug lists (WHO, 2023), and the widely used databases PubChem (PubMed, 2022) and ChEMBL (ChEMBL, 2022).

PubChem is a public chemical database developed by the U.S. National Institutes of Health (NIH), It collects chemical substance descriptions and their biological activities from various sources, including scientific articles and patents, from more than 400 data contributors. PubChem is a key resource for science areas such as cheminformatics, chemical biology, medicinal chemistry, and drug discovery. It contains data about small molecules but also includes other molecular entities such as small-interfering and micro-RNAs, peptides, lipids, carbohydrates, chemically modified macromolecules, and others, all organized into three primary databases: substance, compound, and BioAssay (Kim, 2016).

ChEMBL is an open-access, extensive drug discovery web interface database widely used in academia, industry, and charitable organizations. It contains more than 15 million bioactivity measurements and information extracted from over 67 000 publications, patents, and data exchanged with other databases, such as PubChem, BioAssay, and BindingDB. ChEMBL has accepted direct data deposition since its inception and now contains more than 50 datasets from collaborators, including MMV, DNDi, GSK, and AstraZeneca. To access all the data, ChEMBL enabled users to search for compounds or targets of interest and retrieve bioactivity data through improved free-text searching, interactive filtering, data visualizations, browsing related activity data, and sharing the results of their work by saving the state in the URLs (Mendez et al., 2019).

TABLE 1
Database webpages for target/molecule research

Database	Scope
canSAR	Approved drug curation
Companion diagnostic test	CDX interactions
DRD2/DRD3-GTEx	Gene expression and regulation
Illuminating the druggable genome	Interactions
IUPHAR/BPS	Ligand-activity-target relationships
NCATS pharmaceutical collection	Compounds, bioactivity data
WHOCC-ATC/DDD	Classification system
WHO INN drug lists	Classification system
PubChem	Classification system
ChEMBL	Compounds, bioactivity data
PDB	3D crystal structure
UnitProt	Proteins
BindingDB	Compounds, bioactivity data
PhospoSitePlus	Interactions
IMEx	Interactions
Signor2	Interactions
CCSB	Interactions
Reactome	Interactions
canSynergise	Drug combinations
Pathway Commons	Pathways
DepMap	CRISPR, siRNA
DepMap (CCLE)	Mutations, expression, copy number
MsigDB	Interactions
GDC/TCGA	Mutations, expression, copy number
DEPOD	Interactions
DCC/ICGC	Mutations, expression, copy number
TRRUST	Interactions
TCGA	Mutations, expression
Tfacts	Interactions
DBGET	Pathways, interactions, expression

Source: Each of the listed databases.
Note: Names of drugs database and their scope. ▲

1. 2. The concept of a potential drug

A potential drug is a specific target, structure, or molecular compound identified through initial research. This first approach often involves virtual screening, which uses computational techniques to explore a vast amount of data. Virtual screening is a crucial step in this process, as it allows researchers to quickly and efficiently identify potential candidates from large datasets. If the compound demonstrates promise, it can proceed to the following stages of drug development.

2. Hit discovery by screening

There are two major processes in the discovery of hits by screening: target-based drug discovery and phenotype-based drug discovery, where the primary difference lies in whether the molecular target is identified before or after hit screening. The first steps for target-based drug discovery are target selection, assay development, and biochemical screening. In contrast, the first steps of phenotype-based drug discovery are assay development, cell-based screening, and target deconvolution. Both share the remaining steps: lead optimization, preclinical evaluation, clinical trials, and commercialization (Blay et al., 2020a). These two processes can be considered complementary approaches, involving academic-industrial collaboration, to improve the clinical success rates of new drugs.

2. 1. High-throughput screening

High-throughput screening (HTS) is the predominant strategy for leading discovery used by the pharmaceutical and biotechnology industry. It involves the screening of large chemical libraries (10 000-100 000 compounds per day) against biological targets using automation, miniaturized assays, large-scale data analysis, and other strategies, such as computational techniques and fragment-based drug design (Mayr & Bojanic, 2009). HTS is the most suitable approach when little is known about the target selected for its relevance to the disease. The assays suitable for HTS need to be biologically relevant, sensitive, robust, and cost-effective. HTS formats include: biochemical, binding-based, and cell-based approaches (Blay et al., 2020b). The robustness of the HTS can be assessed using assay quality metrics, such as the Z-factor, a dimensionless coefficient that reflects both the assay signal dynamic range and the data variation associated with the signal measurements, making it suitable for assay optimization and validation (Zhang et al., 1999).

2. 2. Phenotypic screening

Phenotypic drug discovery (PDD) does not rely on knowledge of the identity of a specific target or the hypothesis of its role in disease; on the contrary, PDD is a valuable tool for addressing the complexity of diseases that are poorly understood. PDD is typically conducted using: a cell-based model, an *in vivo* model, a gene-editing tool, organoids, and/or imaging assay technology. These methods are validated by molecular phenotypes that more realistically recapitulate human disease biology. PDD is widely used by both academia and industry, but due to the time-consuming nature and lower costs of the assays, it is more commonly found in academic settings (Horvath et al., 2016; Moffat et al., 2017).

2. 3. Virtual screening or docking

Virtual screening (VS) is used as a cost-effective complement to HTS. It employs a range of computational methods designed for searching large compound databases *in silico*, utilizing both 2D and 3D shape, and selecting a limited number of candidate molecules for testing to identify novel chemical entities with desired biological activity. There are two main types of VS depending on the type of information used to develop the model: structure-based compound screening (docking and de novo design), and ligand-based compound screening (pharmacophore methods, machine learning methods, and chemical-similarity searching based on small molecules). VS is a valuable tool for academia, providing the opportunity to be performed on large online databases, such as those previously described, and/or virtual combinatorial libraries, thereby eliminating the cost of *in vitro*/*in vivo* assays (Bajorath, 2002; Willett, 2006).

2. 4. Fragment screening

Fragment-based drug discovery (FBDD) is an alternative to HTS for the design of small-molecule hit-to-lead compounds. In FBDD, small low-molecular-weight ligands or molecules bind to pockets of various biological targets (in the range of mM to μM). The screening of FBDD requires techniques more sensitive than those used in HTS, as the effects of fragments on proteins are often too weak to be measured using standard assays. Some techniques used in FBDD include: X-ray crystallography, nuclear magnetic resonance, native mass spectrometry, computational approaches, and thermal shift assays, to name a few (Liu & Quinn, 2019; Ohlson & Duong-Thi, 2018).

2. 5. Biomarkers screening

A biomarker is defined as an anatomical, serological, or physiological characteristic that is objectively measured and evaluated as an indicator of a normal biological process, a pathological process, or a biological response to a therapeutic intervention (Atkinson et al., 2001). Biomarker screening relies on biophysiological measurements of organ function as well as imaging, biochemical, and omics technologies (Kraus, 2018). This type of screening can complement PDD by analyzing the associated phenotype of a particular disease.

2. 6. Therapeutic target validation

Target validation involves confirming that the potential drug candidate reaches the target and that this interaction will benefit patients with a given disease while having minimal or acceptable toxicity. This validation step aims to complement the knowledge of a particular target and contribute to reducing the high attrition rates observed in early drug development (Plenge et al., 2013). However, at least 50% of published studies lack reproducibility in industrial laboratories due to various reasons that cause reported results

not to match those obtained by in-house target validation programs of most pharmaceutical companies (Prinz et al., 2011).

Within academic settings, drug discovery strategies such as phenotypic screening, rational design, and data-driven target identification have become increasingly accessible and impactful. The availability of open-access computational platforms and flexible experimental frameworks enables academic researchers to explore novel therapeutic hypotheses with limited resources. However, the translational potential of these discoveries often remains underexploited due to gaps in validation pipelines and limited integration with industrial development processes. Strengthening early-stage collaboration with industry partners is crucial to ensure that academic findings can progress beyond the proof-of-concept stage and contribute meaningfully to the pharmaceutical innovation pipeline.

3. Pharmacophore design

The second general step in the roadmap to drug development is the rational drug design, focusing on the physicochemical characteristics of the molecular structure that exhibits bioactivity on a specific therapeutic target.

3. 1. Pharmacophore modeling

The term pharmacophore refers to a common structural or functional element in a set of compounds that is essential for interaction with a particular biological target macromolecule, thereby triggering, blocking, or mediating its biological response (Langer & Hoffmann, 2006). It also refers to stereo-electronic molecular features rather than functional groups or characteristic structural fragments (Seidel et al., 2020). Pharmacophoric modeling theory is based on the concept that maintaining similar chemical functionalities and spatial arrangement leads to biological activity on the same target. Those pharmacophoric features include: hydrogen bond acceptors (HBA), hydrogen bond donors (HBD), negative ionizable (NI), positive ionizable (PI), hydrophobic entities (H), aromatic entities (AR), and additional size restrictions in the form of a shape or exclusion volumes (XVOL). Pharmacophore models can be generated using two different approaches depending on the source of the data used for the construction of the model: structured-based and the ligand-based pharmacophore modeling; these are widely used in VS and can also be an important tool in scaffold hopping, lead optimization, ligand profiling, target identification, multi-target drug design, or de novo drug design (Giordano et al., 2022).

3. 2. Natural products in drug discovery

Natural products (NPs) are bioactive compounds found in nature that, compared to small synthetic molecules, have higher molecular mass, more

sp3 carbon atoms, more oxygen atoms, more HBD and HBA, greater hydrophilicity, greater molecular rigidity, as well as a lower proportion of nitrogen and halogen atoms (Barnes et al., 2016). NPs as a drug model present limitations, including the process of dereplication, which involves recognizing and excluding already known bioactive compounds from further analysis, as well as data mining and the unambiguous identification of secondary metabolites. Additionally, there is a need for access to sufficient biological material to isolate, characterize, and optimize NPs. NP-based drug research involves biological screening of crude extracts to identify a bioactive "hit", which can be performed by HTS and PDD.

Novel approaches for the biosynthetic development of NPs are based on genome mining. This involves identifying genes that play a key role in the biosynthesis of scaffold structures to identify gene clusters. For instance, BiG-SCAPE (BiG-SCAPE, 2023) is a computational tool that uses a phylogenomic approach in the context of drug discovery. It operates under the assumption that organisms with closer evolutionary relationships are more likely to produce similar NPs (Atanasov et al., 2021). These NPs, despite the challenges inherent to their nature, are a promising tool that offers a vast pool of bioactive molecules, serving as starting points for drug optimization and, ultimately, drug development.

4. *In silico* prediction of pharmacokinetics

A wide array of computational methods is available for predicting regioselectivity, metabolites, drug-metabolizing enzyme interactions, and the toxicological effects of drug metabolism. These methods are distributed as web services and are available as either free or commercial software (Kirchmair et al., 2015a). Based on the 3D structure of macromolecules involved in the pharmacokinetic process, *in silico* techniques aim to predict the binding of small molecules to ADMET-related proteins, their promiscuous characteristics, and off-target related adverse effects.

4. 1. Structure-activity quantitative relation

The Quantitative Structure-Activity Relationship (QSAR) is an *in silico* mathematical model used for pharmacophore design. It aims to find statistical correlations between the structure of the pharmacophore and its function by quantifying the impact of specific structural modifications in existing or predicted molecules. QSAR can be classified from 1D to 6D according to the different dimensions of the descriptors implemented in the method, such as physicochemical properties, structural patterns, 3D structures, ensemble of ligand configurations, induced-fit models, and different solvation models. QSAR is employed as a virtual screening (VS) method in drug discovery to predict the pharmacokinetic and pharmacodynamic profiles of novel compounds (Giordano et al., 2022).

4. 2. Adverse drug reactions

Adverse drug reactions (ADRs) are those events that happen to patients after taking a medication as a part of the clinical treatment and can be categorized into six types from A-F: A (pharmacological effect, predictable and dose-dependent), B (caused by immune and non-immune mediation, nonpredictable and dose-dependent), C (mix pharmaco-immune effect, chronic, cumulative dose-related and manageable by withdrawal), D (dose-related, often caused by drug interaction and manageable by withdrawal), E (withdrawal effect, manageable by slow withdrawal or reintroducing), and F (dose-related therapeutic failure, caused by drug interaction and manageable by changing dose)¸ where type A related to on-target or intrinsic factors and, type B related to off-target of idiosyncratic factors, are the most common (Tong et al., 2021).

4.3. Target promiscuity

Off-target ADRs result from the interaction of a drug or its metabolite (or metabolites) with a non-intended target; these are generally dose-dependent, and some are predictable (Kirchmair et al., 2015b). Chemical similarities between molecules often result in non-specific interactions and unintended activity at off-targets. Target promiscuity can be understood as the percentage of targets hit by drugs (commonly small molecules) at a concentration below 30 μM, compared to the total number of targets tested, such promiscuous drugs are often lipophilic and cationic at physiological pH. Anticipating off-target interactions can be challenging since drugs often modulate off-targets unrelated to their primary target, hence promiscuity can be observed in globally approved drugs and commonly used human drugs that have already been optimized to minimize toxicity (Lounkine et al., 2012).

A previous report has shown the high promiscuity range of small molecules to the principal targets of the safety pharmacology panels used by Big Pharma based on their association with ADRs using the *in silico* similarity ensemble approach (SEA). The most promiscuous target was the voltage-gated sodium channel; most other promiscuous targets were small-molecule-recognizing G-protein-coupled receptors (GPCRs), while transporters exhibited mid-range promiscuity. Enzymes, nuclear receptors, and ligand-gated ion channels were less promiscuous (Lounkine et al., 2012).

Pharmacophore modeling and *in silico* pharmacokinetic prediction are areas where academic institutions demonstrate strong technical capabilities, leveraging computational tools to accelerate candidate selection and reduce experimental costs. These approaches are particularly valuable in early-stage research, where high-throughput screening may be unfeasible. Nonetheless, their full potential depends on integration with experimental validation and alignment with regulatory expectations. Establishing collaborative frameworks with industry can enhance the translational value of academic models, facilitating their adoption in downstream development and regulatory decision-making.

5. Hits optimization

The delivery strategy of drugs depends on the target and the characteristics of the molecule. Oral drugs undergo a series of changes during their pharmacokinetic course and must adhere to specific characteristics known as the 'rule of five' to proceed with drug development. On the other hand, non-oral drugs, specifically biopharmaceutical drugs, consist of complex molecules from NPs or synthetic formulations. These drugs exhibit diverse physicochemical properties and bind to multiple biological targets, making it challenging to predict pharmacokinetics, pharmacodynamics, and pharmacotoxicity.

5. 1. Oral drug optimization

The rule of five predicts that candidate compounds for oral drugs are likely to have unfavorable absorption, permeation, and bioavailability characteristics if they contain more than five hydrogen bond donors (HBD), more than ten hydrogen bond acceptors (HBA), a molecular mass of over 500 Da, and a logP greater than 5 (Lipinski et al., 2012). The first three parameters are fundamental to the protein target's structure and the binding site of the drug. Lipophilicity, described by the logarithm of the octanol/water partition coefficient (logP), indicates the solubility of a compound in a hydrophobic solvent relative to a polar solvent. Unlike the other three parameters, lipophilicity cannot be directly related to target biophysical properties and is often found in NPs (Lipinski, 2016).

5. 2. Optimization of non-oral drugs

Biopharmaceutical drugs offer advantages such as high specificity and potency compared to small molecules due to their structural complexity. However, this complexity also poses challenges for formulation and delivery strategies. To address potential liabilities, such as loss of activity, reduced permeability through biological barriers, instability, and variable viscosity, novel parenteral formulations and delivery strategies have been developed. These include microparticles, depot injections, nanocarriers, jet injections, pumps, transdermal delivery, pulmonary delivery, oral delivery, and other mucosal routes such as vaginal, ocular, nasal, and buccal. While current biopharmaceuticals act on extracellular targets, novel formulations and delivery strategies could result in new classes of biopharmaceuticals with intracellular delivery (Mitragotri et al., 2014).

6. Preclinical assays

Academic work in early drug development during the preclinical phase strongly depends on target-focused *in vitro* assays and *in vivo* animal

models of human diseases. Preclinical assays offer young academic researchers opportunities to obtain preliminary results from basic and applied science, which can be published as academic theses, conference abstracts, and initial papers.

6. 1. *In vitro* safety

In vitro cell-based assay technologies, as part of phenotypic drug discovery, explore target biology and drug mechanisms of action under specific conditions and contexts. Some of these assays include patient-derived diagnostic cell assays, monolayer and non-adherent cell cultures, ex vivo tissue culture assays, induced pluripotent stem cells (iPSCs), gene editing with CRISPR-Cas9 technology, 3D cell culture on organic matrices, 3D microtissues and multicellular spheroid models, inorganic matrix cell culture scaffolds, automated image-based screening platforms, organ-on-a-chip and microfluidics, cellular and molecular analysis, multicellular organotypic and air-liquid interface assays, bioinformatics, image analysis, and image-informatics pipelines (Horvath et al., 2016).

Secondary pharmacology is a crucial component of drug discovery, focusing on *in vitro* safety to achieve optimal specificity of new drugs through hazard identification and off-target mitigation (Whitebread et al., 2016). Four of the major pharmaceutical companies worldwide (AstraZeneca, GlaxoSmithKline, Novartis, and Pfizer) have introduced secondary pharmacology as a standard *in vitro* safety panel to investigate the mode of action and/or effects of molecules not related to their therapeutic target. The panel comprises targets from the GPCR superfamily, ion channel targets, intracellular enzymes, neurotransmitter transporters, nuclear hormone receptors, and a specific kinase. According to a previous report, this approach is based on the most significant impact of secondary pharmacology on drug discovery for the pharmaceutical industry, as off-target mitigation can save patients from unwanted ADRs and the associated cost and undesirable social aspects. *In vitro* pharmacological profiling is a valuable tool for the off-target pharmacological interactions in early drug development (Bowes et al., 2012; Lounkine et al., 2012).

6. 2. Drug pharmacotoxicity

According to previous reports, the number of proteins related to ADRs and toxicological effects is far more than the estimated 324 druggable proteins or biological human targets; there are more than 20 000 human genes, when the previously described pharmacological safety panels only cover ~1.5% of the total genome (Bowes et al., 2012). One of the most relevant proteins on the safety panels is the hERG potassium channel, due to the risk of drug-induced cardiac pro-arrhythmic toxicity it presents. For this interaction, nearly 60% of potential drugs are abandoned. The Comprehensive *in vitro* Proarrhythmia Assay (CiPA) is a clear example of how academic researchers can create a solid

collaboration with the industry, their work together builds a virtual human cardiac model for preclinical *in silico* assays to reduce research and drug development costs with the potential to yield safer medicines (Passini et al., 2021).

6. 3. *In vivo* animal models

When a molecule yields positive results in *in vitro* assays, it is generally followed up with *in vivo* assays. Academia utilizes *in vivo* models of the disease, including cell-derived xenografts (CDX), patient-derived xenografts (PDX), and implantable microdevices, commonly in rats and mice. These models are selected based on their strengths and limitations, including similarities in the tumor microenvironment, low throughput, high cost, and slow development (Flobak et al., 2022).

In vivo genotoxicity testing strategies for efficacy and safety are considered by a working group of the pharmaceutical industry from around the world at the International Workshop on Genotoxicity Testing (IWGT). The 8th IWGT workshop report covers acceptable maximum doses for negative erythrocyte micronucleus (MN) tests, the validation status of MN assays in non-hematopoietic tissues, and nuisance factors in the comet assay (Beevers et al., 2023).

6. 4. Therapeutic index

The Therapeutic Index (TI) is a quantitative relationship between a drug's pharmacology, efficacy, and safety/toxicology. TI is typically considered the ratio that compares the blood concentration or exposure at which the drug causes a therapeutic effect to the highest concentration or exposure to the drug that causes toxicity. During the early drug development process the TI value of the candidate molecule is unknown, an initial TI can be assessed by *in vitro* exposure and calculated as its off-target IC50 divided by its on-target IC50 selectivity; an improved TI can be obtained by predicting the maximum concentration (Cmax), the average concentration across time (Cav), and the area under the concentration-time curve (AUC), as a mathematical calculation that can be validated and challenged with *in vivo* models, where the free drug concentration at the site of action exerts the biological activity (Muller & Milton, 2012).

Despite the growing technical capabilities of academic institutions in early-stage drug development, significant challenges remain in managing the operational and translational risks associated with advancing therapeutic candidates. Academic programs often lack the regulatory expertise, standardized workflows, and risk management strategies commonly found in industry. To address these limitations, the authors propose incorporating experienced personnel, adopting quality standards, and implementing structured project planning from the outset. Integrating such practices within academic environments is crucial for improving reproducibility, reducing attrition rates, and enhancing the likelihood of successful industry collaboration (Ellinger & Gribbon, 2016).

7. Clinical trials

Clinical research involves the study of human subjects to understand both health and disease. The goal is to improve people's health over time through the application of two types of clinical research: observational studies and clinical trials. Observational studies are those in which researchers observe data, such as the habits or environments provided by thousands of patients, and study how these factors affect their health. On the other hand, clinical trials or interventional studies are those in which researchers assign participants to one or more interventions, or to none, to evaluate the biological effects and their health-related outcomes (National Library of Medicine, 2023).

7. 1. Types and phases of clinical trials

There are various types of clinical trials, including prevention trials, screening trials, diagnostic trials, treatment trials, behavioral trials, and quality-of-life trials, also known as supportive care trials. These are conducted in a series of phases, ranging from I to IV, each with a different purpose. Phase I uses around 20-80 people to study the safety and ADRs of the novel molecule; in Phase II the group of people increases to 100-300 and aims to determine effectiveness and safety; Phase III administers the new molecule to 1,000-3,000 people to confirm the efficacy, monitor ADRs, and compares it with the gold standard. Phase IV, or pharmacovigilance, seeks information about the new commercial medicine's benefits in the general population (National Library of Medicine, 2023).

8. Artificial Intelligence and Machine Learning

Artificial Intelligence (AI) and Machine Learning (ML) have revolutionized the field of drug discovery and development, offering innovative solutions to overcome traditional challenges in this process. The integration of these technologies has improved efficiency, reduced costs, and accelerated innovation in the pharmaceutical industry. Artificial Intelligence (AI) refers to the capability of a computer or computer-controlled robot to perform tasks commonly associated with intelligent beings, such as reasoning, learning, and problem-solving. AI encompasses a wide range of technologies, including machine learning, natural language processing, and robotics, which enable machines to mimic human intelligence and perform complex tasks autonomously. Machine Learning (ML) is a subset of AI that focuses on the development of algorithms that allow computers to learn from and make predictions or decisions based on data. ML involves training models using large datasets to recognize patterns and improve their performance over time without being explicitly programmed for each task. Techniques such as supervised learning, unsupervised learning, and reinforcement

learning are commonly used in ML to build predictive models and automate decision-making processes (Ocana et al., 2025).

One of the primary benefits of AI and ML is their ability to analyze vast amounts of data to identify potential therapeutic targets. By leveraging multi-omics data and network-based approaches, these technologies can identify oncogenic vulnerabilities and other critical therapeutic targets that traditional methods may overlook. For instance, models like AlphaFold have demonstrated high accuracy in predicting protein structures, facilitating the assessment of target druggability and structure-based drug design. AI also plays a crucial role in drug design and optimization. Through virtual screening and de novo design techniques, AI algorithms can generate molecular structures optimized for specific biological properties. This not only accelerates the drug discovery process but also enhances the precision and efficacy of the designed compounds. Additionally, AI aids in ligand optimization and structure-based design processes, resulting in a higher success rate in identifying promising drug candidates (Koçak & Akçalı, 2025).

In the early stages of clinical development, AI and ML significantly improve clinical trial design and patient selection. By analyzing electronic health records, these technologies can efficiently identify and recruit suitable patients for clinical trials. Furthermore, AI can optimize trial protocols and use predictive models to adapt trial strategies, such as synthetic control arms and digital twins, which simulate outcomes using real or virtual patient data. These innovations help mitigate logistical and ethical challenges while enhancing the accuracy and relevance of clinical trials (Konski, A. F. & Foley & Lardner LLP, 2025).

AI and ML have the potential to transform drug discovery and development, improving efficiency and accelerating innovation. Integrating these technologies into current processes, while requiring collaboration and high-quality data, can offer innovative solutions to traditional challenges in the pharmaceutical industry.

9. Collaboration and multidisciplinary efforts between academia and industry

Collaboration between academia and the pharmaceutical industry is crucial for accelerating the discovery of new molecules and the development of drugs. This collaborative effort combines the deep scientific knowledge and innovative capacity of academic researchers with the financial resources and expertise in the development and commercialization of the industry. Academia, with its focus on basic research and exploration of new biological mechanisms, can identify and validate promising therapeutic targets. On the other hand, the industry can bring these discoveries into practice by developing and optimizing compounds for clinical use (Cheng et al., 2020).

A notable example of a structured academic initiative that bridges the gap between discovery and application is the DRIVE model (Drug Innovation Ventures at Emory), developed at Emory University. This hybrid framework combines the scientific creativity of academia with the operational rigor of industry, incorporating elements such as intellectual property management, regulatory planning, and early-stage investment strategies. By adopting a professionalized infrastructure within the academic environment, DRIVE enables the advancement of promising therapeutic candidates beyond proof of concept, facilitating their progression into clinical development. This model illustrates how educational institutions can maintain scientific leadership while actively contributing to the pharmaceutical innovation pipeline through the development of translational and commercially viable outputs (Liotta & Painter, 2018).

Translational medicine plays a crucial role in this process, as it focuses on translating basic research findings into clinically relevant applications that benefit patients. This approach requires sustained and close collaboration between academic scientists and industry professionals to ensure that discoveries can be effectively scaled and applied. For example, academic scientists can develop predictive models and conduct preclinical studies, while the industry can provide the necessary resources to carry out clinical trials and meet regulatory requirements (Yu et al., 2024). A notable example of this collaboration is the development of gene therapies, where academic research on genetic mechanisms has been translated into innovative clinical treatments with the support of the industry (Ramadan et al., 2023).

Moreover, multidisciplinary efforts are fundamental to addressing the complex challenges of drug development. Teams that include biologists, chemists, pharmacologists, engineers, and regulatory experts work together to design, test, and optimize new treatments. This interdisciplinary collaboration enables the integration of knowledge and skills essential to overcoming obstacles in drug development. The combination of different perspectives and experiences facilitates innovation and improves the efficiency of the development process, from molecule identification to drug commercialization (DrugBank Team, 2024).

The emergence of hybrid translational research centers has introduced a promising paradigm for bridging the gap between academic discovery and industrial application. Recent publications describe how these professionalized environments combine academic innovation with industrial-grade operational standards, enabling more efficient target validation, compound optimization, and the generation of preclinical proof-of-concept. By integrating scientific creativity with structured project management and regulatory awareness, such models enhance the translational potential of academic research. Their implementation represents a strategic opportunity to overcome institutional limitations and foster sustainable, high-impact collaborations between academia and the pharmaceutical sector (Nussbaumer & Klebl, 2015).

9. 1. Collaborative projects between academia and industry

One of the most prominent examples of collaboration between academia and industry is the gene therapy project for spinal muscular atrophy developed by Novartis and the University of Oxford. In this project, Novartis provided funding and expertise in clinical trial design and regulatory affairs. At the same time, the research team at the University of Oxford led the development of gene therapy technology. This type of collaboration leverages the strengths of both parties to accelerate the development of innovative treatments (Lewis, 2025).

Another significant example is the Lilly-Purdue 360 initiative, which aims to accelerate innovation across all stages of the pharmaceutical supply chain. This collaboration involves the application of AI-driven tools to enhance traditional drug discovery methods, as well as the utilization of robotics and data science to scale manufacturing capacity more effectively. The initiative also focuses on workforce development, ensuring a continuous flow of talent to meet the demands of Lilly and other employers in Indiana (Lilly Investors, 2025).

Additionally, the collaboration between industry and academia in the development of mRNA vaccines is a notable example of how academic research can be translated into commercially viable products with a significant public health impact. Academic laboratories, led by scientists like Katalin Karikó, developed mRNA technology, which was then commercialized by companies like Moderna and Pfizer/BioNTech to combat the COVID-19 pandemic (Cowling & Thielemans, 2020).

These projects demonstrate how collaboration between academia and industry can accelerate the development of new treatments and improve the efficiency of the drug discovery and development process.

10. Ethical aspects in drug discovery, development, and commercialization

Ethical considerations are paramount throughout the entire process of drug discovery, development, and commercialization. Ensuring ethical practices at every stage not only safeguards the well-being of participants and patients but also maintains public trust in both academia and the pharmaceutical industry.

10. 1. Preclinical Testing

Preclinical testing involves evaluating the safety and efficacy of potential drug candidates before they are tested in humans. Ethical considerations here include the humane treatment of animals and the responsible use of data. Researchers must ensure that their studies are designed to minimize harm and maximize benefits. Ethical principles such as respect for persons, beneficence, and justice guide these efforts. For example, the use of animal models must adhere to strict guidelines to ensure humane treatment,

including providing comfortable living conditions, proper nutrition, and access to veterinary care (Shamoo & Resnik, 2022).

10. 2. Clinical Trials

Clinical trials are a critical phase in drug development, involving human participants to test the safety and efficacy of new drugs. Ethical considerations in clinical trials are extensive and include informed consent, risk-benefit analysis, and the protection of vulnerable populations. Participants must be fully informed about the nature of the trial, its risks, and potential benefits before they agree to participate. Researchers must also ensure that the selection process for participants is fair and does not exploit vulnerable populations. Additionally, ethical oversight by independent committees is essential to monitor the conduct of the trials and ensure compliance with ethical standards (Van Campen et al., 2021).

10. 3. Post-Approval and Commercialization

Once a drug is approved and commercialized, ethical considerations continue to play a crucial role in its development and use. Pharmaceutical companies must ensure that their marketing practices are responsible and do not mislead patients or healthcare providers. Accurate information about the drug, including potential side effects and benefits, must be provided. Pricing strategies also raise ethical concerns, as high drug prices can limit patient access to essential medications. Companies must balance the need to recoup research and development (R&D) costs with the ethical obligation to make drugs affordable and accessible (Mackie et al., 2006).

10. 4. Continuous Ethical Oversight

Ethical oversight does not end with commercialization. Continuous monitoring of the drug's performance and safety in the market is essential. Post-marketing surveillance helps identify any adverse effects that may not have been apparent during clinical trials. This ongoing vigilance ensures that any issues are promptly addressed, maintaining the safety and efficacy of the drug for patients (Finegold & Moser, 2006).

10. 5. Ethical considerations in academia and industry

Both academia and the pharmaceutical industry have a shared responsibility to uphold ethical standards throughout the drug development process. Collaboration between these sectors can sometimes lead to moral dilemmas, such as conflicts of interest or differing values. However, fostering an ethical culture in both settings enhances scientific integrity and builds public trust. Academia focuses on basic research and education, while the industry emphasizes applied research and commercialization. By working together and adhering to ethical principles, both sectors can contribute to the development of safe and effective drugs that benefit society (Shamoo & Resnik, 2022).

Perspectives

The outlook presented by this work is auspicious, emphasizing the pivotal role academia plays in the early stages of drug development, a field continuously shaped by scientific and technological innovation. As biomedical challenges become increasingly complex, academic institutions are not only generating fundamental knowledge but also developing rational strategies and computational models to enhance the search for novel therapies. Tools such as phenotypic screening, pharmacophore design, and *in silico* pharmacokinetics prediction help reduce both time and cost, thereby democratizing access to sophisticated methods that were once exclusive to the pharmaceutical industry.

Growth is anticipated in hybrid models of academic-industrial collaboration, such as translational research centers, which professionalize scientific environments without compromising academic creativity. These models facilitate therapeutic target validation, molecular refinement, and the generation of preclinical proof-of-concept, bolstering the transition from basic research to clinical development. Moreover, the integration of artificial intelligence and machine learning provides a transformative lens, enabling the reinterpretation of complex datasets and accelerating compound discovery. In this scenario, academia may lead not only through knowledge generation but also through ethical innovation, upholding transparency and methodological rigor. Through multidisciplinary training, open-source computational tools, and strategic partnerships, academic institutions are poised to become cornerstones of the global pharmaceutical ecosystem. Ultimately, this work envisions an integrative approach where academia not only participates but actively reshapes the drug development paradigm—constructing a robust bridge between discovery and tangible clinical impact.

Conclusion

Collaboration between academia and the pharmaceutical industry is crucial for advancing drug discovery and development. The integration of advanced technologies such as artificial intelligence and machine learning has significantly improved efficiency, reduced costs, and accelerated innovation. However, it is crucial to address the gap between academic results and their industrial application to maximize the impact of these collaborations. Additionally, ethical considerations must be prioritized at every stage of the process to ensure safety and public trust. By combining academic precision with industrial implementation capabilities and fostering an ethical, multidisciplinary approach, we can achieve transformative advances in medicine. From the educational perspective, the next step is to strengthen translational research, promote the formation of interdisciplinary teams, and explore emerging technologies to optimize drug development, thus ensuring a promising future in pharmaceutical innovation.

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Declaración de autoría (CRediT):

Sarah Eliuth Ochoa Hugo: conceptualización, curación de datos, análisis formal, investigación, metodología, administración del proyecto, redacción-borrador original, redacción-revisión y edición.